- 2 -

## LISTING OF THE CLAIMS

Claim 1 (currently amended) A method for the production of a single heavy chain antibody in a transgenic non-human mammal comprising the step of expressing a heterologous VHH heavy chain locus in that mammal specifically in B cells in response to antigen challenge, wherein the VHH heavy chain locus is integrated into the non-human mammal's genome and said VHH heavy chain locus comprises:

- (a) at least one VHH exon, at least one D exon and at least one J exon, wherein the VHH exon, the D exon and the J exon are capable of recombining to form a VDJ coding sequence, and wherein the VHH exon comprises a naturally occurring VHH coding sequence,
- (b) a constant heavy chain region comprising at least one  $C\mu$  constant heavy chain gene and at least one of  $C\gamma$ ,  $C\alpha$ ,  $C\epsilon$ , or  $C\delta$  constant heavy chain gene, wherein each of said constant heavy chain genes, when expressed, does not express a functional CH1 domain,
- (c) a locus control region ("LCR") providing for expression of the VHH heavy chain locus specifically in B cells

said method comprising:

- 1) immunizing said mammal with an antigen and
- 2) isolating single heavy chain antibody against said antigen.

Claims 2 - 6 (canceled)

Claim 7 (currently amended) The method of claim 1 or 41 wherein the VHH single heavy chain locus comprises a camelid VHH, at least one D exon of human origin, [[and]] at

PATENT

DOCKET NO.: CARP0015-101 APPLICATION SERIAL NO. 10/692,918

- 3 -

least one J exon of human origin, and a constant region of human origin.

Claims 8 - 9 (canceled)

Claim 10 (previously presented) The method of claim 1 or 41 wherein the constant heavy chain region comprises at least one constant region heavy chain gene which is of noncamelid origin.

Claim 11 (original) A method according to claim 10 wherein at least one constant region heavy chain gene is of human origin.

Claims 12 - 32 (canceled)

Claim 33 (previously presented) The method of claim 1 or 41 wherein the entire VHH single heavy chain locus is of camelid origin

Claims 34-36 (canceled)

Claims 37 -38 (canceled)

Claim 39 (previously presented) The method according to claim 1 or 41 wherein the non-human mammal is a rodent.

Claim 40 (canceled)

Claim 41 (currently amended) A method for the production of a single heavy chain antibody in a transgenic mouse comprising expressing a heterologous VHH heavy chain locus in said mouse specifically in B cells in response to antigen challenge wherein the VHH heavy chain locus is integrated into the non-human mammal's genome and said VHH heavy chain locus comprises:

(a) at least one VHH exon, at least one [[-D]] D exon and at least one [[-J]] J exon, wherein

-4-

the VHH exon, the D exon and the J exon are capable of recombining to form a VDJ coding sequence, and wherein the VHH exon comprises a naturally occurring VHH coding sequence, and

- (b) a constant heavy chain region comprising at least one  $C\mu$  constant heavy chain gene and at least one of  $C\gamma$ ,  $C\alpha$ ,  $C\epsilon$ , or  $C\delta$  constant heavy chain gene, wherein each of said at least one constant heavy chain gene, when expressed, does not express a functional CH1 domain,
- (c) a regulatory sequence providing for expression of the VHH heavy chain locus specifically in B cells

said method comprising:

- 1) immunizing said mammal with an antigen and
- 2) isolating single heavy chain antibody against said antigen.

Claim 42 (canceled)

Claim 43 (previously presented) The method of claim 1 or 41 wherein said antibody is isolated using hybridoma technology.

Claim 44 (previously presented) The method of claim 1 or 41 wherein said antibody comprises a variable region fragment and said variable region fragment is isolated using phage display.